ECLAMPSIA AND PREECLAMPSIA:

Background

- Hypertension –most common medical disorder in pregnancy
- Affects 6-10 % pregnancy worldwide
- 2nd most common cause of maternal deaths
- Worldwide :14 % pregnancy related deaths (Global cause of maternal deaths :WHO systemic analysis
- Nepal :The incidence of preeclampsia or eclampsia was 20 cases to one thousand hospital deliveries.

Classification

- Gestational Hypertension
- Preeclampsia
  - Preeclampsia without severe features
  - Severe
- Chronic Hypertension
- Chronic Hypertension with superimposed preeclampsia.

American College of Obstetricians and Gynecologists Task force on Hypertension in Pregnancy. Hypertension in pregnancy. ACOG. Washington, DC, 2013.

Definitions

- **Gestational Hypertension:** Elevated Blood pressure without proteinuria after 20 wks of gestation . Resolves by 12 weeks post partum
- **Preeclampsia** : New onset of hypertension and proteinuria after 20 wks gestation.
- **Chronic hypertension** : Systolic BP ≥ 140 mm Hg and/or Diastolic BP ≥ 90 mmHg or Elevated BP that fails to resolve after delivery.
- **Chronic hypertension with superimposed preeclampsia**: Preeclampsia develops in woman with chronic HTN before pregnancy. Diagnosed by new onset of proteinuria or a sudden increase in proteinuria or HTN or both
- **HELLP Syndrome** : Hemolysis, elevated liver enzymes, low platelet count in woman with preeclampsia.
- **Eclampsia** : CNS involvement with new onset of seizures in woman with preeclampsia.

Preclampsia

- **Preeclampsia without Severe Features**
  - Hypertension ≥ 140/90 mm Hg beyond 20 weeks
  - Proteinuria (spot protein creatinine ratio >0.3 or 24h urine collection >300mg protein or 1+ on urine dipstick)
- **Severe Preeclampsia**
  - Hypertension ≥ 160/110mmHg
  - Thrombocytopenia (platelet count <1,00,000/mm3)
  - Serum Cr >1.1mg/dl or >2 times the baseline serum Cr
  - Pulmonary edema
  - Impaired liver function
  - New onset cerebral or visual disturbances

BOX 36-3 Risk Factors for Preeclampsia

Demographic Factors

- Advanced maternal age > 35 years
- Black race
- Hispanic ethnicity

Genetic Factors

- History of preeclampsia in previous pregnancy
- Family history of preeclampsia
- History of placental abruption, fetal growth restriction, or fetal death
- Partner who fathered a preeclamptic pregnancy in another woman (through fetal genes)

Medical Conditions

- Obesity
- Chronic hypertension
- Diabetes mellitus
- Chronic renal disease
- Antiphospholipid antibody syndrome
- Systemic lupus erythematosus

Obstetric Conditions

- Multiple gestation
- Hydatidiform mole

Behavioral Factor

- Cigarette smoking (risk reduction)

Partner-Related Factors

- Nulliparity
- Limited preconceptional exposure to paternal sperm*

Pathogenesis

- Preeclampsia as two-stage disorder
  - **Asymptomatic 1st stage –** in early pregnancy with impaired remodeling of spiral arteries
  - **Symptomatic 2nd stage –** characterized by release of antiangiogenic factors from intervillous space to maternal circulation

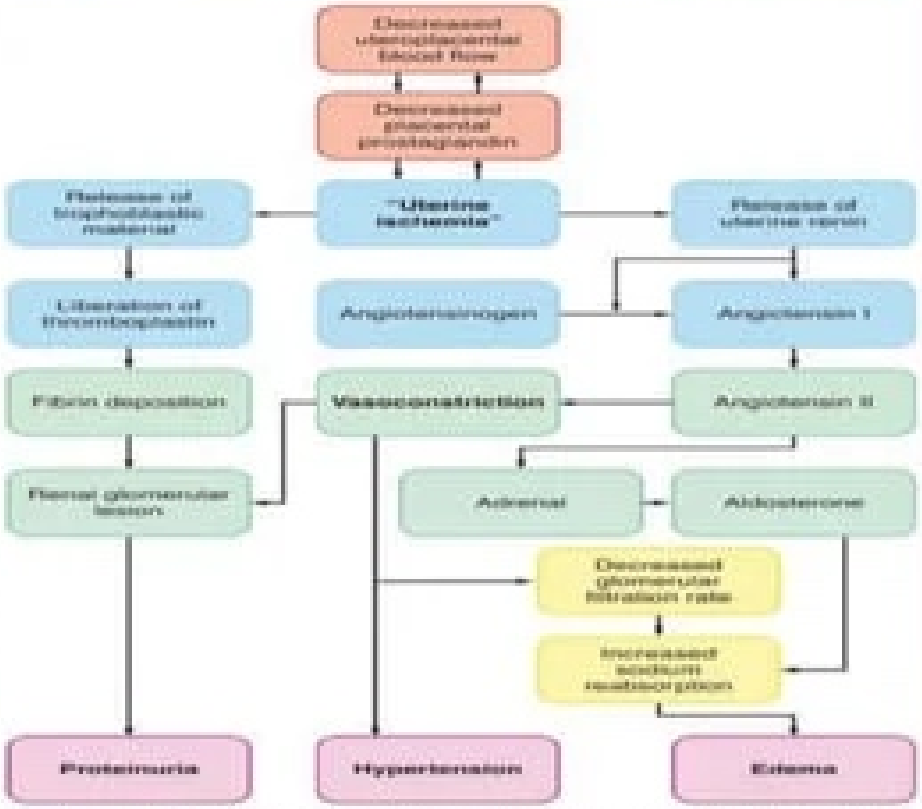


FIGURE 40-3. Proposed scheme of pathophysiologic changes in toxemia of pregnancy. (Reprinted from: Spenoff L. Toxemia of pregnancy. Mechanism and therapeutic management. Am J Cardiol. 1973;32:582, with permission.)

Pathogenesis contd..

- **Normal Pregnancy**
- Embryo-derived cytotrophoblasts invades decidual and myometrial segments of spiral arteries.

↓

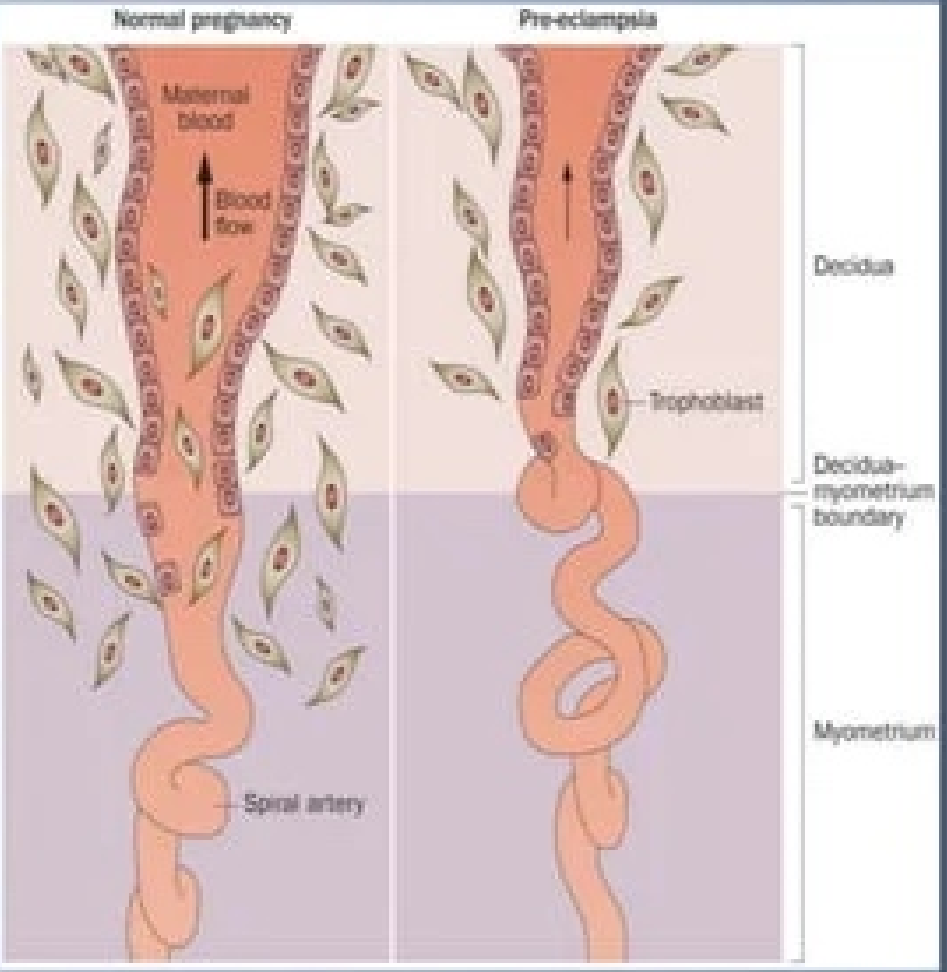
- Remodeling of vascular smooth muscle and inner elastic lamina.

↓

- Luminal diameter of spiral arteries ↑ , creating low-resistance vascular pathway to intervillous space.

↓

- Ensure adequate blood flow to nourish growing fetus and placenta



Pathogenesis contd..

Cytotrophoblast invasion is incomplete and only decidual segment undergo change

↓

Results in abnormal superficial placentation.

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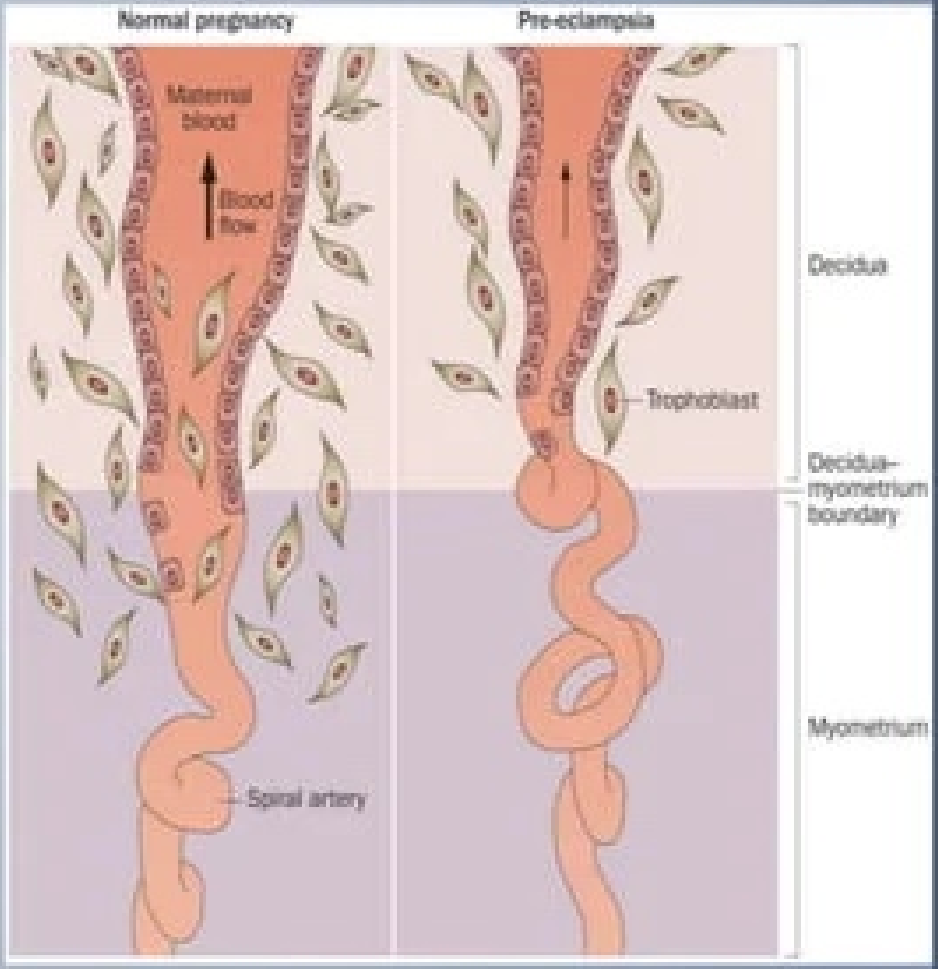
↓ placental perfusion and placental infarcts, predisposing to IUGR.

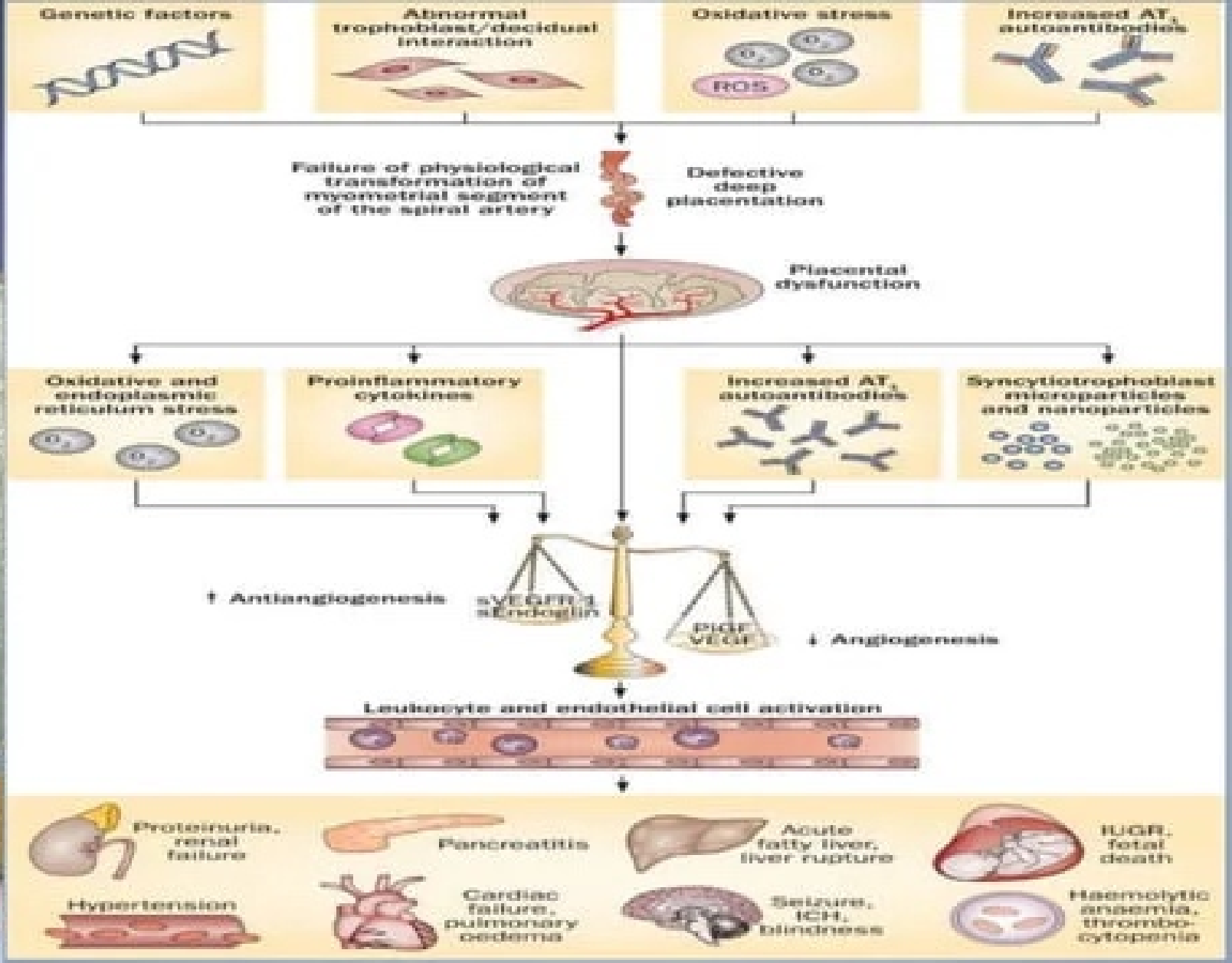
↓

Symptomatic 2nd stage

↓

Widespread maternal endothelial dysfunction and systemic inflammatory response.




Genetic factors
Abnormal trophoblast/decidual interaction
Oxidative stress
ROS
Increased AT_1 autoantibodies
Failure of physiological transformation of myometrial segment of the spiral artery
Defective deep placentation
Placental dysfunction
Oxidative and endoplasmic reticulum stress
Proinflammatory cytokines
Increased AT_1 autoantibodies
Syncytiotrophoblast microparticles and nanoparticles
↑ Antiangiogenesis
sVEGFR-1
sEndoglin
PlGF
VEGF
↓ Angiogenesis
Leukocyte and endothelial cell activation
Proteinuria, renal failure
Pancreatitis
Acute fatty liver, liver rupture
IUGR, fetal death
Hypertension
Cardiac failure, pulmonary oedema
Seizure, ICH, blindness
Haemolytic anaemia, thrombo-cytopenia

Clinical Features

Neurological
- Headache
- Visual disturbances
- Hyperexcitability
- Seizures
- Intracranial hemorrhage
- Cerebral edema

Pulmonary
- Upper airway edema
- Pulmonary edema

Cardiovascular
- Decreased intravascular volume
- Increased arteriolar resistance
- Hypertension
- Heart failure

Clinical features

Hepatic
- Impaired function
- Elevated enzymes
- Hematoma
- Rupture

Renal
- Proteinuria
- Sodium retention
- Decreased glomerular filtration
- Renal failure

Hematological
- Coagulopathy
- Thrombocytopenia
- Platelet dysfunction
- Prolonged partial thromboplastin time
- Microangiopathic hemolysis

Uteroplacental Perfusion

Activity increased
Hyperactive/hypersensitive to oxytocin
Preterm labor – frequent
Uterine/placental blood flow – decreased by 50-70%
Abruption – incidence increased
IUGR

Management Of Preeclampsia

› **Obstetrics management**

1. Maternal and fetal surveillance
2. Treatment of acute hypertension
3. Seizure prophylaxis
4. Decisions regarding route and time of delivery

Maternal And fetal surveillance

- Indicated in all the preeclamptic patients.
- **Goal:** early detection of severe disease in preeclampsia without severe features and in case of severe preeclampsia - to detect worsening of organ dysfunction.
- Evaluate for Sign and symptoms indicating end-organ involvement,

TABLE 36-3 **Initial Laboratory Investigations for Women in Whom Hypertension Develops after 20 Weeks' Gestation**

Test	Rationale
Hemoglobin and hematocrit	Hemoconcentration supports diagnosis of preeclampsia and is an indicator of severity. Values are decreased if hemolysis is present.
Platelet count	Thrombocytopenia suggests severe preeclampsia.
Urine protein-creatinine ratio or 24-h urine protein excretion	Presence of proteinuria distinguishes preeclampsia from gestational hypertension.
Serum creatinine level	Abnormal or rising creatinine level suggests severe preeclampsia, especially in presence of oliguria.
Serum aminotransferase levels	Elevated serum aminotransferase levels suggest severe preeclampsia with hepatic involvement.

Modified from Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. Am J Obstet Gynecol 2000; 183:S1-S22; and American College of Obstetricians and Gynecologists Taskforce on Hypertension in Pregnancy. Hypertension in pregnancy. ACOG. Washington, DC. 2013.

Maternal and fetal contd..

1. Daily fetal movement counts with NST or biophysical profile testing at time of diagnosis and at regular intervals thereafter.
2. USG: fetal weight and AF volume.
3. Doppler USG: measure fetal blood flow velocimetry when IUGR is suspected.

Treatment of Acute Hypertension

- Antihypertensive used to treat severe HTN (SBP≥160 mmHg or DBP ≥110mmHg)
- **Goal of therapy** :Prevent adverse maternal sequences like hypertensive encephalopathy, Cerebro vascular hemorrhage, Myocardial infarction , and CCF.
- **Aim** : lower MAP by 15- 25%, with target SBP between 120- 160 mm Hg and DBP between 80-105 mm Hg.

TABLE 36-4 Treatment of Acute Severe Hypertension* In Preeclampsia/Eclampsia

Medication	Onset of Action†	Dose
Labetalol	5-10 min	20 mg IV, then 40-80 mg every 10 min up to maximum dose of 220 mg IV
Hydralazine	10-20 min	5 mg IV every 20 min up to maximum dose of 20 mg IV
Nifedipine	10-20 min	10 mg PO every 20 min up to a maximum dose of 50 mg
Nicardipine	10-15 min	Initial infusion 5 mg/h, increase by 2.5 mg/h every 5 min to a maximum of 15 mg/h
Sodium nitroprusside‡	0.5-1 min	0.25-5.0 µg/kg/min IV infusion

ACOG 2011 Recommends Labetalol or Hydralazine as 1st line treatment for acute onset, severe HTN in pregnancy or postpartum patients

Seizure prophylaxis

- Routinely used for seizure prophylaxis
- Magnesium sulphate: Loading dose of 4 to 6 g over 20- 30 mins followed by maintenance of 1 to 2 g/h.
- Infusion initiated once decision is made to deliver and continued for 24 hours postpartum.
- Some recommend $MgSO_4$ at least 2 hrs before cesarean, during surgery, and for 12 hours postpartum.

Seizure prophylaxis contd..

- Mechanism of direct anticonvulsant not well understood
- It may protect Blood brain barrier
- Decrease cerebral edema
- Act centrally at n-methyl –D- aspartate (NMDA) receptors to raise seizure threshold

Route of Delivery

- Vaginal delivery should be attempted PE without severe features or in severe disease beyond 34 wks.
- Cesarean delivery: when maternal or fetal condition mandates immediate delivery

- **Corticosteroid therapy:**
- For Severe PE or HELLP syndrome
- To accelerate fetal lung maturity
- Between 24-34 weeks

Anesthetics Management

› Preanesthetic Evaluation

- History
- Airway examination
- Maternal hemodynamics
- Coagulation status
- Fluid balance

Anesthetic Management

› **Monitoring**

- Standard ASA monitor
- Invasive BP, CVP-??
- Urine output
- Uterine contraction monitor
- Continuous fetal heart rate monitoring

Neuraxial Analgesia For Labor and Delivery

Lumbar Epidural/ CSE

- Avoid GA and possibility of airway catastrophe and stress response with airway manipulation
- Improvement in intervillious blood flow
- Provision of high quality analgesia
- Reduction of catecholamines and stress related hormones
- Extended analgesia if emergency cesarean required
- Excellent post op analgesia.

Special considerations

- Assessment of coagulation status.
- IV hydration before the epidural administration of LA.
- Treatment of hypotension.
- Avoid use of epinephrine-containing LA solutions.

Guidelines for Central Neuraxial Block

- Neuraxial block may be initiated if platelet count >80,000/mm3.
- Platelet count between 50,000 and 80,000/mm3, weigh risks and benefits of CNB with GA.
- <50000 – avoid neuraxial blockade
- Platelet count 80000-100000 –early epidural catheter insertion recommended in anticipation of worsening thrombocytopenia
- Plt count of 75000-80000/mm3 –reasonable for epidural catheter removal.

Chestnut's Obstetrics Anesthesia Principles And Practice-5th Edition, page number 844-845

Anesthesia for Caesarean Delivery

› Special concerns

1. Choice of anesthetic technique
2. Technique for induction of GA
3. Interaction between $MgSO_4$ and NDMR

Anesthesia for Cesarean delivery

General anesthesia:

Indications

- Coagulopathy
- Sustained fetal bradycardia with reassuring maternal airway
- Severe ongoing maternal hemorrhage
- Contraindications to neuraxial technique

Anesthesia for cesarean delivery

› *Three specific challenges of GA*

- Potential difficult of securing airway
- Hypertensive response to laryngoscopy
- Effects of $MgSO_4$ in on Neuromuscular transmission and uterine tone

BOX 36-5 A Suggested Technique for Administration of General Anesthesia in Women with Severe Preeclampsia

1. Place a radial arterial cannula for continuous blood pressure monitoring in women with severe hypertension.
2. Place an additional large-bore intravenous catheter given the increased risk for postpartum hemorrhage.
3. Verify that smaller-sized endotracheal tubes and supraglottic airway devices are immediately available. Equipment needed for difficult airway management should also be immediately available.
4. Consider the administration of an H_2-receptor antagonist and metoclopramide IV between 30 and 60 minutes before induction of anesthesia.
5. Administer 0.3 M sodium citrate 30 mL by mouth less than 30 minutes before induction of anesthesia.
6. Denitrogenate (3 minutes of tidal-volume breathing or 8 vital capacity breaths with an F_{IO_2} of 1.0 and a tight-fitting facemask).
7. Give labetalol (10-mg bolus doses) IV to titrate systolic blood pressure to 140/90 mm Hg before the induction of anesthesia.
8. Continue to monitor the FHR during labetalol administration.
9. Consider alternative antihypertensive agents for patients who do not respond to labetalol (or those with a contraindication to labetalol). Alternatives include hydralazine or nicardipine, sodium nitroprusside, or nitroglycerin infusion. Consider remifentanil infusion at 0.05 μg/kg/min. (See Table 36-4.)
10. Perform rapid-sequence induction with propofol 2.0 to 2.8 mg/kg and succinylcholine 1.0 to 1.5 mg/kg (avoid ketamine as an induction agent given its sympathomimetic properties). Consider the administration of a bolus dose of labetalol, esmolol, nitroglycerin, sodium nitroprusside, or remifentanil to blunt the hemodynamic response to laryngoscopy.
11. Maintain anesthesia with a volatile halogenated agent and 100% oxygen before delivery. After delivery, decrease the concentration of the volatile halogenated agent to prevent uterine atony and consider using nitrous oxide or a propofol infusion and administering an opioid with or without a benzodiazepine. Avoid giving additional muscle relaxants; if absolutely required, administer a *low dose* of a short-acting nondepolarizing muscle relaxant because of the exaggerated effect of these medications when coadministered with magnesium.
12. At the end of surgery, reverse neuromuscular blockade and give labetalol 5 to 10 mg IV bolus, titrated to effect, to prevent hypertension during emergence and tracheal extubation.

Anesthetic concern with MgSO4

- Potentiation and prolongation of action of both depolarizing, non-depolarizing muscle relaxants.
- At higher doses Mg^{2+} rapidly crosses the placental barrier, has been found to significantly ↓ FHR variability.
- Should be given cautiously with Ca^{2+} as may antagonize the anticonvulsant effect of $MgSO_4$.
- Also be cautious in patients with renal impairment.
- May ↑ the possibility of hypotension during regional block .

Postoperative Management

- **Post op analgesia:**

  IV opioids, neuraxial opioids, epidural analgesia

  Concern : Respiratory depression

  NSAIDS: avoid

- **Post partum management:**

Risk of

Pulmonary Edema	Sustained hypertension
Stroke	Venous thromboembolism
Airway obstruction	Seizures
HELLP	PPH
	Eclampsia

HELLP Syndrome

- Occurs in 70% antepartum cases and 30% postpartum
- **Signs and Symptoms**
  - Right upper quadrant or epigastric pain
  - Nausea and vomiting
  - Headache
  - Hypertension
  - Proteinuria

TABLE 36-6 Diagnostic Criteria for Hemolysis, Elevated Liver Enzymes, and Low Platelets (HELLP) Syndrome

Criteria	Laboratory Tests
Hemolysis	Abnormal peripheral blood smear Increased bilirubin > 1.2 mg/dL Increased LDH > 600 IU/L
Elevated liver enzyme levels	Increased AST ≥ 70 IU/L Increased LDH > 600 IU/L
Thrombocytopenia	Platelet count < 100,000/mm^3

LDH, lactic dehydrogenase; *AST*, aspartate aminotransferase.
Modified from Sibai BM. The HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets): much ado about nothing? Am J Obstet Gynecol 1990; 162:311-6.

Management of HELLP Syndrome

- Assess and Stabilize mother (1st priority)
  - Antihypertensive
  - Anti seizure prophylaxis
  - Correct coagulation abnormalities.
- Assess fetal condition- FHR, Doppler USG, biophysical profile
- Ultimate Management
  - >34 wks gestation →deliver
  - <34wks →expectant Management if stable maternal and fetal conditions
- Platelet transfusion if:

  <40,000/mm^3 before cesarean delivery

Eclampsia

- New onset of seizures or unexplained coma during pregnancy or postpartum period in woman with s/s of PE and without a preexisting neurologic disorder.
- Can occur any point in puerperium
- 0.1 to 5.9/ 10,000 pregnancies in developed countries.
- Most seizures occur intrapartum or within 1st 48 hours after delivery.
- **Late eclampsia** :Seizure onset from 48 hours after delivery to 4 weeks postpartum.

Risk Factors

- Maternal age < 20 yrs
- Nulliparity
- Multigravida
- Molar pregnancy
- Triploidy
- Pre-existing HTN, Renal /CVS disease
- Previous severe PE or Eclampsia
- Nonimmune hydrops fetalis
- SLE

Pathogenesis

› Poorly understood

Involve a loss of normal cerebral autoregulatory mechanism

⬇

Hyperperfusion and leading to interstitial and vasogenic edema and decreased cerebral blood flow

Complications

- Pulmonary aspiration
- Pulmonary edema
- CVA
- Cardiopulmonary arrest
- Venous thromboembolism
- Acute renal failure
- Death

Obstetrics Management

- **Immediate Goals**
- Stop convulsion
- Establish patent airway
- Prevent major complications i.e hypoxemia ,aspiration
- **Further goals**
- Antihypertensives
- Induction or augmentation of labor
- Expeditious delivery

Management

BOX 36-6 Eclampsia: The ABCs of Eclamptic Seizure Control

AIRWAY

- Turn patient to left side; apply jaw thrust.
- Attempt bag and mask ventilation ($FIO_2 = 1.0$).
- Insert soft nasopharyngeal airway if necessary.

BREATHING

- Continue bag and mask ventilation ($FIO_2 = 1.0$).
- Apply pulse oximeter and monitor SpO_2.

CIRCULATION

- Secure intravenous access.
- Check blood pressure at frequent intervals.
- Monitor electrocardiogram.

DRUGS

- Magnesium sulfate
  - 4 to 6 g IV over 20 min
  - 1 to 2 g/h IV for maintenance therapy
  - 2 g IV over 10 min for recurrent seizures
- Antihypertensive agents
  - Labetalol or hydralazine as needed to treat hypertension (see Table 36-4)

MgSO4 Therapy

- **Zuspan regimen: 4-6g iv over 15 min f/b infusion of 1-2g/h**
- **Pritchard regimen:** 4g i.v over 3-5min f/b 5g in each buttock with maintenance of 5g im in alternate buttock 4hrly
- **MOA**:Competitive inhibition of calcium ions at motor end plate or cell membrane, ↓ Ach release & sensitivity
- **C/I**:Patients with MG and impaired renal function, heart block, digitalis
- **S/E**:Maternal : flushing
- Perspiration, headache, muscle weakness, pulmonary edema
- Neonatal: lethargy, hypotonia, respiratory depression

MgSO4 level :

- Normal Serum levels- 1.7- 2.4 mEq/l
- Therapeutic range- 5- 9 mEq/l
- Patellar reflex lost- >12 mEq/l
- Respiratory depression- 15-20 mEq/l
- Cardiac arrest- >25 mEq/l

MgSO4 toxicity

› Stop infusion.

› IV Cal. gluconate10 ml 10% over 10 minutes.

Anesthetic Management

- Maintenance of Fluids : 75-100 ml/hr.
- Assessment of seizure control and neurologic function.
- BP control : If BP ≥160/110 mmHg.
- Monitoring :ASA stand., FHR, UO, NM and Mg monitoring
- CBC, RFT, LFTs, Coagulation profile, 24 hrs specimen for protein
- Choice of anesthesia: GA with STP or Propofol
- Avoid hypo/hyperventilation, hyperglycemia, hypoxia, hyperthermia

Choices of anesthesia in Eclampsia

Central Neuraxial

- Seizures controlled
- No coagulopathy
- Co-operative pt

General Anesthesia

- Uncontrolled seizures
- Coagulopathy
- Reassuring airway
- Uncooperative patients

REFERENCES

- Chestnut's Obstetrics Anesthesia Principles And Practice-5th Edition
- Morgan & Mikhail's Clinical Anesthesiology 5th Edition